図 5-c. 変形性股関節症例の三次元 CT 像
左股関節側面（臼底部）
大腿骨頭を外したイメージ

図 5-d. 変形性股関節症例の三次元 CT 像
左股関節側面
大腿骨頭を外したイメージ
この画像上で各種の計測が可能

出力されたSTLデータをもとに三次元CAD（Computer Aided Design：コンピュータ支援設計）立体デザインシステムを利用して三次元データを一定間隔の厚みをもったスライスデータに変換した。各スライスを順番に積み重ねることで、三次元データと同じ形状の実物モデルを作製した（図 6）。

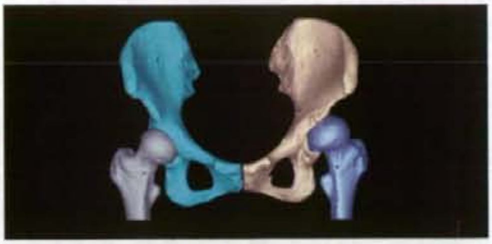

図 6-a. 三次元 CAD で作製した
形状データ
両股関節正面

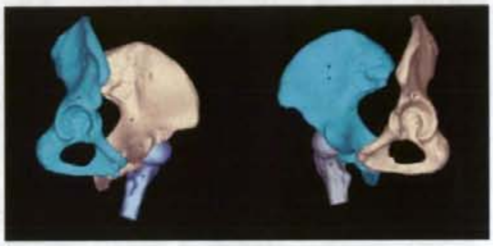

図 6-b. 三次元 CAD で作製した
形状データ
両股関節側面

図 6-c. 三次元 CAD で作製した
形状データ
骨盤・骨頭のイメージ

これら CAD モデルデータを STL フォーマットに変換し、インクジェット粉末積層装置を利用し立体モデルを作製した（三次元積層造形法）。このモデルでは、

以後の人工股関節手術シミュレーションのことを考慮し、石膏を粉体として使用した（図7）。

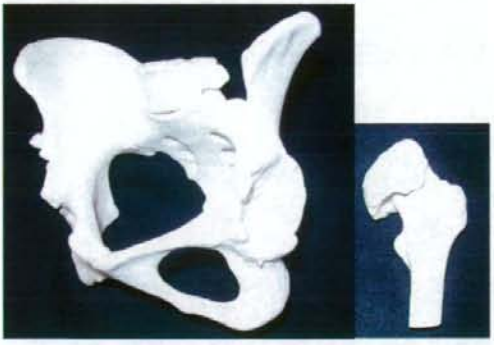

図7. 三次元変形性股関節症モデル

そして、これらの三次元変形性股関節症モデルに人工股関節手術シミュレーションを行い、コンポーネント形状の検討を開始した（図8）。

図8-a. 三次元変形性股関節症モデルに対する人工股関節手術シミュレーション
（臼蓋コンポーネント）

図8-b. 三次元変形性股関節症モデルに対する人工股関節手術シミュレーション
（大腿骨コンポーネントおよび関節摺動面）

D. 考察

本研究において、三次元 Computer Aided Design（CAD）立体デザインシステム、三次元積層造形法（ラピッドプロトタイピング）を用い、4症例について石膏製の変形性股関節症三次元モデルを作製することができた。

手術シミュレーションには、術者のイメージを容易に補完する立体モデルを用いる方法と、コンピュータ仮想空間での方法がある。コンピュータシミュレーションには高価な設備投資が必要であるが、立体モデルはハンドリングに長けており臨床の場で利点がある。しかし、従来の三次元モデルの欠点は作製にコストが高く、かつモデルの材質が生体骨の感触とかけ離れているという点であった。このため、モデルに手術手技を加えた場合、容易に破損する脆弱性や、硬度が高すぎるなどの理由で、実際の手術で使用する器具（ノミやボーンソー、高速回転バー、ドリル、ラスプなど）を用いることが不可能であった。本研究で作製した変形性股関節症三次元モデルの

大きな特色は、石膏を用いることでモデルの特性を形態の模倣から脱却し、形態＋生体特性の維持という一歩前進させたことにある。この特色をいかし、実際の手術器具および人工股関節インプラントを用い、手術のシミュレーションを行うことが可能であった。次年度以降は、このモデルを使用し、臼蓋コンポーネント、ライナー、大腿骨コンポーネント等、インプラントのデザインに改良を加え、関節摺動面の安定性・吸着性を向上する新しい人工股関節の形状を検討する予定である。

E. 結論

変形性股関節症患者のCT画像を元に、当該患者の承諾を得て、三次元Computer Aided Design (CAD) 立体デザインシステム、三次元積層造形法（ラピッドプロトタイピング）を用い石膏製の変形性股関節症三次元モデルを作製した。次年度以降はこのモデルを用いて手術のシミュレーションを行い、関節摺動面の安定性・吸着性を向上する新しいインプラントの形状検討する予定である。

F. 健康危険情報

特になし。

G. 研究発表

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H. 知的財産権の出願・登録状況

なし

別紙4

研究成果の刊行に関する一覧表レイアウト

雑誌

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Enhanced Wear Resistance of Orthopaedic Bearing Due to the Cross-Linking of Poly(MPC) Graft Chains Induced by Gamma-Ray Irradiation

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Abstract: We assumed that the extra energy supplied by gamma-ray irradiation produced cross-links in 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted cross-linked polyethylene (CLPE-*g*-MPC) and investigated its effects on the tribological properties of CLPE-*g*-MPC. In this study, we found that the gamma-ray irradiation produced cross-links in three kinds of regions of CLPE-*g*-MPC: poly(MPC) layer, CLPE-MPC interface, and CLPE substrate. The dynamic coefficient of friction of CLPE-*g*-MPC slightly increased with increasing irradiation doses. After the simulator test, both the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC cups exhibited lower wear than the untreated CLPE ones. In particular, the gamma-ray sterilized CLPE-*g*-MPC cups showed extremely low and stable wear. As for the nonsterilized CLPE-*g*-MPC cups, the weight change varied with each cup. When the CLPE surface is modified by poly(MPC) grafting, the MPC graft polymer leads to a significant reduction in the sliding friction between the surfaces that are grafted because water thin films formed can behave as extremely efficient lubricants. Such a cross-link of poly(MPC) slightly increases the friction of CLPE by gamma-ray irradiation but provides a stable wear resistant layer on the friction surface. The cross-links formed by gamma-ray irradiation would give further longevity to the CLPE-*g*-MPC cups. © 2007 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 84B: 320–327, 2008

Keywords: joint replacements; polyethylene; phosphorylcholine; sterilization

INTRODUCTION

The number of primary and revised artificial hip and knee joints used are substantially increasing in the world every year.[1] This means that the quality of artificial joints has been becoming increasingly important. Most of the patients who receive an artificial joint experience a dramatic pain relief and enjoy a rapid improvement in the quality of life. The most popular artificial joint system is a bearing couple composed of an ultra-high molecular weight polyethylene (UHMWPE) and Co-Cr-Mo alloy. However, osteolysis caused by wear particles of UHMWPE has emerged as a serious issue.[2–4] The reduction in the number of UHMWPE wear particles is a method to prevent osteolysis. From this viewpoint, different combinations of bearing surfaces and improvement in the bearing materials have been focused upon.

We have recently developed a novel artificial joint system with 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted onto the surface of cross-linked polyethylene (CLPE-*g*-MPC),[5–7] aiming to reduce wear and avoid bone resorption. MPC is a methacrylate monomer that has a phospholipid polar group in a side chain and is used to make novel biomaterials as designed by Ishihara et al., who were inspired by the natural phospholipids of biomembranes.[8] MPC can be a good polymer biomaterial owing to

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the reduction of protein adsorption and cell adhesion.[9–18] On the basis of the biocompatibility and hydrophilicity of MPC polymers, we have been developing new artificial joints with highly lubricated bearing surfaces that are produced by photo-induced radical graft polymerization.[19] This technique grafts MPC directly onto CLPE, forming C—C covalent bonds between the CLPE substrate and the MPC polymer.

Medical devices, including artificial joints, are normally sterilized by using several methods, for example, gamma-ray sterilization, ethylene oxide gas sterilization, and gas plasma sterilization. In particular, gamma-ray irradiation is the sterilization method typically used for the UHMWPE components of artificial joints. However, gamma-ray sterilization probably influences the properties of medical devices. Generally, when a high energy beam generated by gamma-ray sterilization is irradiated on to a polymer, free radicals are formed by the scission of the molecular chains. This is followed by the retermination and cross-linking of the molecules. The irradiation of high-dose gamma-rays onto UHMWPE severs the C—C or C—H bonds, and it then produces cross-linking and subsequent chemical bonding involving C═O and C—C.[20] It has been reported that gamma-ray sterilized UHMWPE sometimes exhibits improved wear resistance due to the formation of many cross-links. Several investigators have reported that wear resistance is better in gamma-ray sterilized UHMWPE than that in ethylene oxide sterilized UHMWPE.[21–24]

The purpose of this study is to investigate the dependence of gamma-ray irradiation on the tribological (friction and *in vitro* wear) properties of CLPE-*g*-MPC and to examine the possibility of controlling the longevity of artificial joints by using this material. This is based on the hypothesis that the extra energy supplied by gamma-ray irradiation could produce cross-links in CLPE-*g*-MPC.

MATERIALS AND METHODS

Chemicals and MPC Graft Polymerization

Benzophenone and acetone were purchased from Wako Pure Chemical Industries (Osaka, Japan). MPC was industrially synthesized using the method reported by Ishihara et al.[8] and was supplied by Ai Bio-Chips (Tokyo, Japan).

A compression-molded UHMWPE (GUR1020 resin, Poly Hi-Solidur, IN) bar stock was treated with a dose of 50 kGy gamma irradiation in N_2 gas and annealed at 120°C for 7.5 h in N_2 gas in order to attain cross-linking. The CLPE specimens were machined from this bar stock after cooling. They were immersed in an acetone solution containing 10 mg/mL benzophenone for 30 s and then dried in the dark at room temperature to remove acetone. The amount of benzophenone adsorbed on the surface was 3.5×10^{-11} mol/cm^2.[25] The MPC monomer was dissolved in pure degassed water up to a concentration of 0.5 mol/L. The CLPE specimens coated with benzophenone were immersed in the aqueous MPC solution. The photo-induced graft polymerization on the CLPE surface was carried out with an ultraviolet irradiation (UVL-400HA ultra-high pressure mercury lamp, Riko-Kagaku Sangyo, Funabashi, Japan) of 5 mW/cm^2 at 60°C for 90 min using a filter (Model D-35; Toshiba, Tokyo, Japan) to pass only ultraviolet light with a wavelength of 350 ± 50 nm. After the polymerization, the CLPE-*g*-MPC specimens were removed, washed with pure water and ethanol, and dried at room temperature. The CLPE and CLPE-*g*-MPC specimens were sterilized by gamma-ray irradiation of 25 or 50 kGy in N_2 gas.

Surface Analysis by Fourier-Transform Infrared and X-ray Photoelectron Spectroscopies and Water-Contact Angle Measurement

The functional group vibrations of both the nonsterilized and gamma-ray sterilized CLPE and CLPE-*g*-MPC surfaces were examined by Fourier-transform infrared (FTIR) spectroscopy using attenuated total reflection (ATR) equipment. The FTIR/ATR spectra were obtained in 32 scans over a range of 800–2000 cm^{-1} using an FTIR analyzer (FT/IR-615; JASCO International, Tokyo, Japan) at a resolution of 4.0 cm^{-1}.

The surface elemental conditions of CLPE before and after MPC grafting were analyzed by X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS Hsi 165; Kratos Analytical, UK) equipped with an Mg-Kα radiation source at 15 kV at the anode. The take-off angle of the photoelectrons was kept at 90°. Each sample was scanned five times.

The static water-contact angles of CLPE-*g*-MPC with various photo-polymerization periods were measured by a sessile drop method using an optical bench-type contact angle goniometer (Model DM300; Kyowa Interface Science, Saitama, Japan). Drops of purified water (1 μL) were deposited onto the surface of CLPE-*g*-MPC, and the contact angles were directly measured by using a microscope after 60 s according to the ISO 15989 standard.[26] Fifteen replicate measurements were performed on each sample, and the average values were taken as contact angles.

Friction Test

The friction test was performed using a ball-on-plate machine (Tribostation 32; Shinto Scientific, Tokyo, Japan). Six sample pieces were prepared using each of the sterilization methods. The Co-Cr-Mo alloy ball was 9 mm in diameter and its surface roughness was Ra ≥ 0.01—as smooth as a femoral ball. The friction tests were carried out with a load of 0.98 N and a sliding distance of 25 mm with a frequency of 1 Hz at room temperature. The measurements were performed using pure water as lubricant. The friction tests were performed up to a maximum of 100 cycles. The mean static (μ_s) and dynamic (μ_d) coefficients of friction were determined by averaging five data points in 10 (8–12) and 100 (96–100) cycle measurements.

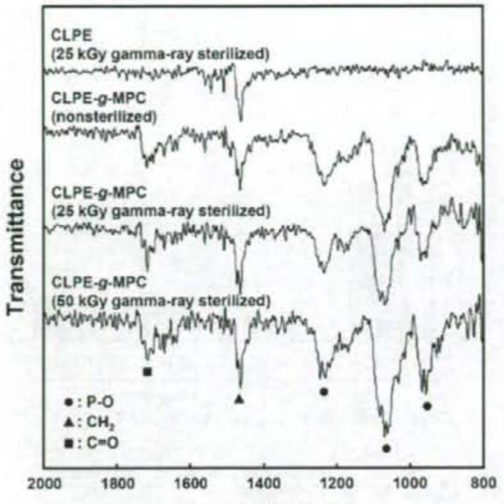

Figure 1. FTIR/ATR spectra for nonsterilized and gamma-ray sterilized CLPE and CLPE-*g*-MPC.

Statistical Analysis

For the water-contact angle measurement and friction test, the results derived from each measurement were expressed as mean values and the standard deviation. The statistical significance ($p < 0.05$) was judged by the Student's *t*-test.

Hip Joint Simulator Test

The inner and outer diameters of the CLPE and CLPE-*g*-MPC cups used in the hip joint simulator were 26 and 52 mm, respectively. Four pieces for each condition was prepared. The wear test was performed using a 12-station hip joint simulator (MTS Systems, MN). A Co-Cr-Mo alloy femoral ball component with a size of 26 mm (Japan Medical Materials, Osaka, Japan) was used as *a femoral* component. A mixture of 25 vol % bovine serum, 20 mM/L of ethylene diamine tetraacetic acid (EDTA), and 0.1 mass % sodium azide was used as lubricant, according to the ISO 14242-1 standard.[27] The lubricant was replaced every 0.5 $\times 10^6$ cycles. Loads simulating a physiologic loading curve with double peaks of 1793 and 2744 N loads were applied with a frequency of 1 Hz. The wear was determined by weighing the polyethylene cups. Load-soak controls ($n = 2$) were used to compensate the fluid absorption of specimens. The weights of the cups were measured every 0.5×10^6 cycles. Then, the testing was continued until a total of 5.0×10^6 cycles were completed.[28]

To evaluate the wear conditions, the surface features of the bearing surfaces of the cups were observed with a confocal laser scanning microscope (OLS1200; Olympus, Tokyo, Japan) after a simulator test with 5.0×10^6 cycles.

RESULTS

Figure 1 shows the FTIR/ATR spectra for the nonsterilized and gamma-ray sterilized CLPE and CLPE-*g*-MPC. An absorption peak was observed at 1460 cm^{-1} for both CLPE and CLPE-*g*-MPC. This peak is attributed mainly to the methylene chain in the CLPE substrate and MPC graft polymer. However, the transmission absorptions at 1240, 1080, and 970 cm^{-1} were observed only for the CLPE-*g*-MPC. These peaks are due to the phosphate group in the MPC unit. Similarly, an absorption peak at 1720 cm^{-1} observed for CLPE-*g*-MPC only corresponds to the carbonyl group in the MPC unit. The FTIR/ATR spectra did not differ significantly between the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC.

Table I summarizes the elemental compositions of the untreated CLPE and the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Both the elemental composition of nitrogen and phosphorous in the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surface were approximately 5.2. It should be noted that the contents of nitrogen and phosphorous in the CLPE-*g*-MPC surface remained unchanged after gamma-ray sterilization. The elemental composition of the CLPE-*g*-MPC surface was almost equivalent to the theoretical elemental composition (N = 5.3, P = 5.3) of poly(MPC). On the other hand, the carbon content in the gamma-ray sterilized CLPE-*g*-MPC slightly increased as compared with that of the nonsterilized one.

Figure 2 shows the static water-contact angle of the untreated CLPE and the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. The static water-contact angle

TABLE I. Surface Elemental Composition (%) of Gamma-Ray Sterilized CLPE and CLPE-*g*-MPC

Sample (Sterilization Method)	Surface Elemental Composition (%) ($n = 5$)			
	C	O	N	P
CLPE (nonsterilized)	99.8 (0.3)[a]	0.2 (0.3)	0.0 (0.0)	0.0 (0.0)
CLPE (25 kGy γ-sterilized)	99.5 (0.2)	0.6 (0.2)	0.0 (0.0)	0.0 (0.0)
CLPE (50 kGy γ-sterilized)	99.1 (0.2)	0.9 (0.2)	0.0 (0.0)	0.0 (0.0)
CLPE-*g*-MPC (nonsterilized)	58.0 (0.2)	31.5 (0.2)	5.2 (0.1)	5.3 (0.1)
CLPE-*g*-MPC (25 kGy γ-sterilized)	63.7 (2.3)	26.0 (2.3)	5.2 (0.1)	5.1 (0.2)
CLPE-*g*-MPC (50 kGy γ-sterilized)	65.0 (0.6)	24.6 (0.5)	5.2 (0.1)	5.2 (0.1)
MPC polymer[b]	57.9	31.6	5.3	5.3

[a] The standard deviation is in parentheses.
[b] Theoretical elemental composition of MPC polymer.

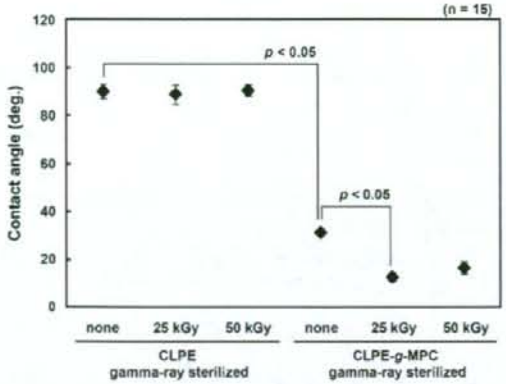

Figure 2. Static water-contact angle of the untreated CLPE and the nonsterilized and the gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar; Standard deviations.

of the untreated CLPE was approximately 90° before and after gamma-ray sterilization, and it drastically decreased (approximately 30°) because of MPC grafting. Furthermore, the static water-contact angles of CLPE-*g*-MPC decreased to 15° after gamma-ray sterilization.

The static and dynamic coefficients of friction of gamma-ray sterilized CLPE and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC are shown in Figures 3 and 4. Both the static and dynamic coefficients of friction of CLPE-*g*-MPC decreased drastically when compared with those of untreated CLPE. The degree of reduction in the coefficient was larger in the latter as compared to the former. Considering the gamma-ray sterilized CLPE-*g*-MPC, regardless of the dose of the gamma-ray sterilization and the cycles, approximately 50% reduction (i.e., 46–65%) was observed in the static coefficients of friction for both the 10 and 100 cycles when compared with those of untreated CLPE. On the other hand, the dose of gamma-ray sterilization affected the dynamic coefficient of friction of CLPE-*g*-MPC. That is, it slightly increased from 0.007 (none) to 0.021 (50 kGy) with an increase in the gamma-ray sterilization dose for 10 cycles. The dynamic coefficient of friction of CLPE-*g*-MPC with gamma-ray sterilization of 50 kGy was 75% greater ($p < 0.05$) than that of CLPE-*g*-MPC with nonsterilization.

Figure 5 shows the weight change (gravimetric wear) of the gamma-ray sterilized CLPE cups and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC cups in the hip joint simulation test. When the gravimetric method is used, the weight loss was corrected for the fluid absorption by sub-

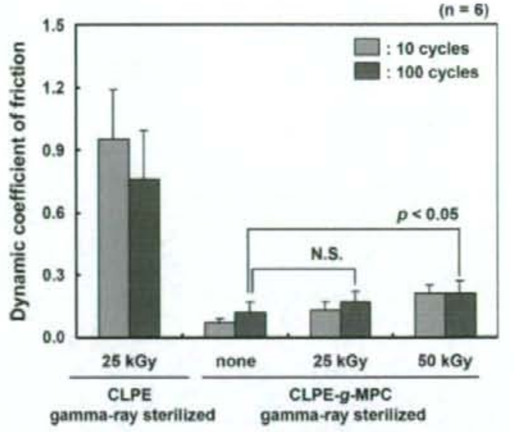

Figure 4. Dynamic coefficients of friction of gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar; Standard deviations.

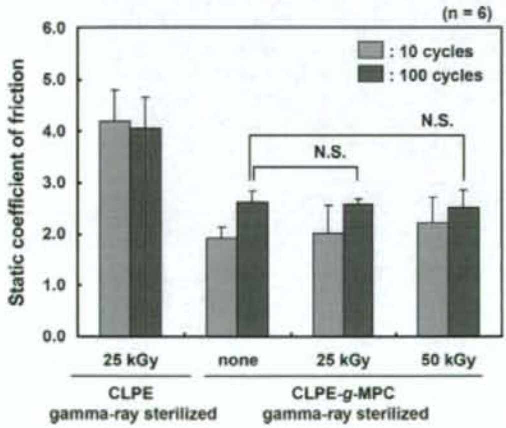

Figure 3. Static coefficients of friction of the gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar; Standard deviations.

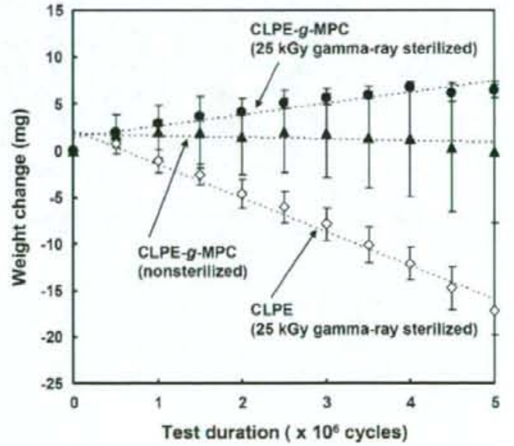

Figure 5. Weight change (gravimetric wear) of gamma-ray sterilized CLPE cups and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC cups in the hip joint simulation test. Bar; Standard deviations.

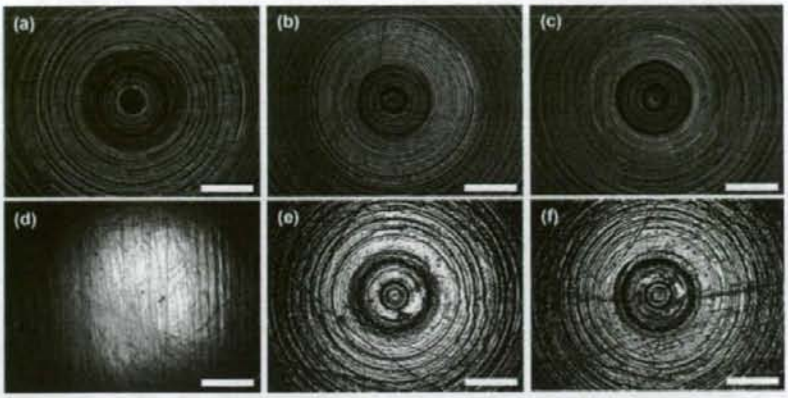

Figure 6. Confocal laser scanning microscope images of the CLPE and CLPE-*g*-MPC bearing surfaces before and after the hip simulator test. (a) CLPE (gamma-ray sterilized), (b) CLPE-*g*-MPC (nonsterilized), (c) CLPE-*g*-MPC (gamma-ray sterilized) before the hip simulator test, (d) CLPE (gamma-ray sterilized), (e) CLPE-*g*-MPC (nonsterilized), and (f) CLPE-*g*-MPC (gamma-ray sterilized) after the hip simulator test. The bar indicates 500 μm.

tracting the weight gain that occurred in the load-soak controls. Since the tested cups are subjected to a motion and load, such a "load-soak" correction is not necessarily satisfactory. Therefore, the tested cups absorb slightly more fluid than their load-soak controls. Consequently, the correction for using the load-soak control data may result in a slight underestimation of the actual weight loss. After 5.0 $\times$ 10^6 cycles of the simulator test, both the CLPE-*g*-MPC cups were found to undergo lesser wear than the untreated CLPE cups. In particular, the gamma-ray sterilized CLPE-*g*-MPC cups showed extremely low and stable wear. As for the nonsterilized CLPE-*g*-MPC cups, the weight change varied for each cup (standard deviation = 7.6 mg, $n = 4$). Figure 5 indicates that certain gamma-ray sterilized CLPE-*g*-MPC cups exhibit a slight increase in weight because of slightly enhanced fluid absorption when compared with that in the load-soak controls.

Figure 6 shows the confocal laser scanning microscope images of the bearing surfaces of the untreated gamma-ray sterilized CLPE cups and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC cups before and after the simulator test. Before the simulator test, regular circular machining marks were seen on the all the bearing surfaces of the CLPE and CLPE-*g*-MPC cups. After the simulator test, the machining marks on these surfaces of the CLPE cups disappeared completely. On the contrary, clear machining marks with regular circles were observed on the surface of the nonsterilized and gamma-ray sterilized CLPE-*g*-MPC cups, indicating almost no wear on the surface.

DISCUSSION

We have developed an artificial hip joint using CLPE-*g*-MPC on the bearing surface with an objective of reducing wear and avoiding bone resorption. The static and dynamic coefficients of friction of CLPE-*g*-MPC reduced by >50% and >90%, respectively, as compared to those of the untreated CLPE, as shown in Figures 3 and 4. These friction coefficients were much lower than those usually found for the measurable shear interactions between UHMWPE and the Co-Cr-Mo alloy.[29,30] The significant reduction in the coefficients of friction of the grafted MPC polymer resulted in a substantial improvement in wear resistance, as shown in Figure 5. We assumed that the bearing surface of the artificial hip joint combined with the MPC polymer layer 100–200 nm thick exhibited the fluid film lubrication (or mixed lubrication) of the intermediate hydrated layer.[5,7,19]

These sterilizations may affect the properties of medical devices. Generally, when a high energy beam by gamma-ray sterilization is irradiated on a polymer, free radicals are formed by the scission of molecular chains.[20] This is followed by the retermination and cross-linking of the molecules. In this study, we therefore assumed that the extra energy supplied by gamma-ray irradiation produced cross-links in three kinds of regions of the CLPE-*g*-MPC: poly (MPC) layer, CLPE-MPC interface, and CLPE substrate, as shown in Figure 7.

As shown in Table I, the contents of nitrogen and phosphorous in the CLPE-*g*-MPC surface were hardly different between the nonsterilized CLPE-*g*-MPC and the gamma-ray sterilized CLPE-*g*-MPC. On the other hand, the contents of carbon and oxygen of CLPE-*g*-MPC slightly increased and decreased (as a trade-off), respectively, with an increase in the gamma-ray irradiation dose. It was assumed that the energy by gamma-ray irradiation would be used in the scission of C=O in the MPC structure by the degassing of O_2 and subsequently produce cross-links of poly(MPC) with chemical bonding involving C—C.[31,32] The extra energy supplied by gamma-ray sterilization of 25–50 kGy is clearly responsible for producing more cross-links.

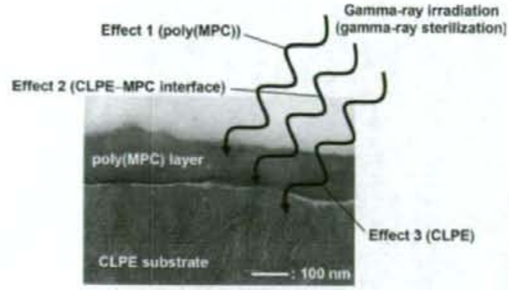

Figure 7. Schematic diagram of the effects of gamma-ray irradiation on CLPE-*g*-MPC.

The dose of gamma-ray sterilization influences the friction response since the dynamic coefficient of friction of CLPE-*g*-MPC slightly increased from 0.007 to 0.021 within the low friction region with an increase in the gamma-ray sterilization dose. It was previously reported that as the polymer concentration (viscosity) increases with the increase in the friction coefficient in the mixed lubrication regime.[33] It was therefore assumed that an ultra-low friction of CLPE-*g*-MPC that appeared during sliding is related to the effective viscosity of poly(MPC) in the mixed lubrication of the intermediate hydrated layer. The viscosity of poly(MPC) reflects the mobility of the free end groups of the MPC polymer or MPC polymer chains themselves; this mobility was limited by the cross-linking of poly(MPC) layer.[34,35] These results seem to suggest that the cross-link corresponds to the viscosity of the poly(MPC) in the bearing interface, the viscosity of the poly(MPC) increases by gamma-ray irradiation, and the poly(MPC) would act as a boundary lubricant in mixed lubrication. These effects are represented as "Effect 1" in Figure 7.

After 5.0×10^6 cycles of the simulator test, the gamma-ray sterilized CLPE-*g*-MPC cups showed low and stable wear (Figure 5). On the contrary, with the nonsterilized CLPE-*g*-MPC cups, the weight change varied in each cup. In the previous study, when a high energy beam was irradiated onto a polymer with a grafted layer, strong bindings were formed between the grafted layer and polymer substrate.[36] Lewis et al. reported that the force required to remove the coating with cross-linking was greater than that without cross-linking.[37] In addition, much more cross-linking and perhaps adhesion to the substrate was induced by the gamma-ray irradiation (gamma-ray sterilization) when compared with the nonsterilized CLPE-*g*-MPC. It is therefore assumed that the higher energy radiation in gamma-ray sterilization induced cross-links not only within the grafting MPC polymer but also between the grafting MPC polymer and CLPE substrate. Then, a much stronger and stable MPC polymer grafted layer was produced on the bearing surface ("Effect 2" in Figure 7).

McKellop et al. reported on the wear performance of UHMWPE in a contemporary hip simulator following gamma-ray irradiation in air as well as in an inert gas and ethylene oxide gas sterilization or gas plasma sterilization.[21] Between 2 and 5×10^6 cycles, the wear rate of the gamma-ray sterilized UHMWPE was significantly lower than that of the UHMWPE sterilized either by gas plasma or ethylene oxide. A similar trend has been reported by Wang et al. who observed more than 50% drop in the hip simulator wear rate after single 25 kGy doses of gamma-ray sterilization.[22] These studies have reported that the wear resistance is better in gamma-ray sterilized UHMWPE than in ethylene oxide sterilized UHMWPE.[21–24] It is therefore assumed that gamma-ray irradiation improved the wear resistance of the CLPE substrate ("Effect 3" in Figure 7).

In the cross-link process of this study, the UHMWPE bar stock was irradiated with a dose of 50 kGy, and then CLPE and CLPE-*g*-MPC were gamma-ray sterilized with a nominal dose of 25 kGy. Thus, the total dosage for the gamma-ray sterilized CLPE and CLPE-*g*-MPC was 75 kGy. The nonsterilized CLPE-*g*-MPC received a total dose of 50 kGy only; this would be a disadvantage for the anti-wear property.[38–40] However, as shown in Figure 6, clear machining marks with regular circles remained on the surfaces of the nonsterilized as well as gamma-ray sterilized CLPE-*g*-MPC cups even after the simulator test. The observed CLPE-*g*-MPC cups were virtually unworn, which is consistent with the relatively low wear in the hip joint simulator tests, as shown in Figure 5. In contrast, the machining marks disappeared from the surface of the gamma-ray sterilized CLPE cups [Figure 6(b)]. In other words, the presence of poly(MPC) on the CLPE surface by MPC grafting would have a greater effect on the wear resistance than the additional cross-links of the CLPE substrate by the gamma-ray irradiation of 25 kGy. The CLPE surface with the poly(MPC) exhibited considerably higher lubricity than that without the poly(MPC) (Figures 2–4). The significant reduction in the coefficient of friction of the grafted poly(MPC) resulted in a substantial improvement in wear resistance. The bearing surface of the artificial hip joint combined with poly(MPC) might exhibit the fluid film lubrication (or mixed lubrication) of the intermediate hydrated layer. This means that artificial hip joints utilizing CLPE-*g*-MPC mimic the natural joint cartilage.[41,42]

The concern about the degradation of polyethylene during shelf aging prompted several orthopedic manufacturers to adopt the sterilization method using gas plasma or ethylene oxide gas for conventional UHMWPE.[43,44] These sterilization methods admittedly generate no free radicals that could be subsequently oxidized during shelf storage. However, UHMWPE sterilized using these methods did not receive the tribological benefit associated with radiation-induced cross-linking. Moreover, the oxidation index of the degraded polyethylene was lower *in vivo* than *in vitro*.[21,45] It has also been reported that the oxygen content might be almost zero in the body.[44,46] Thus, although the oxidation degradation of polyethylene *in vivo* is related to the surrounding oxygen concentration, that is, that of the body fluid, it is not a main factor of the degradation as a whole. However, recent studies reported that conventional or cross-linked gamma-ray sterilized polyethylene liners undergo *in vivo* oxidation, especially in unworn bearing surface regions and the rim. In contrast, the oxidation of a worn bearing surface was not observed.[47] On the basis of these studies, we assumed that when oxygen is excluded from the package during sterilization, further cross-linking, and additional improvement in the wear performance are attained. However, we must pay attention to the rim fracture in CLPE-*g*-MPC cup by the possible impingements based on the abovementioned studies.[47] In the previous study, for gamma-ray irradiation, the lower molecular weight cross-linked GUR1020 materials had higher mechanical properties (tensile and impact properties) for all doses as compared to the higher molecular weight cross-linked GUR1050 materials.[48] Therefore, we selected a GUR1020 compression-molded bar stock as the CLPE substrate. Nevertheless, the cross-linked GUR1020 materials showed the same wear rate as the cross-linked GUR1050 materials.

Gamma-ray sterilization has had a long history and it has been one of the most popular sterilization methods for various medical products to date. A barrier package has been widely adopted to satisfactorily address the historical problem of the oxidation of gamma-ray sterilized products during shelf storage. In this study, we confirmed that the extra energy supplied by gamma-ray irradiation produced cross-linking in the three regions of the CLPE-*g*-MPC: poly(MPC) layer, CLPE-MPC interface, and CLPE substrate. When the CLPE surface is modified by poly(MPC) grafting, the MPC graft polymer leads to a significant reduction in the sliding friction between the surfaces which are grafted because water thin films formed can act as extremely efficient lubricants. Gamma-ray sterilized CLPE-*g*-MPC showed a slightly higher friction than the nonsterilized one. However, the wear resistance is more stable in the former than in the latter. The cross-links formed by gamma-ray irradiation would give further longevity to CLPE-*g*-MPC cups. Based on the mechanical,[19] biological,[5,49,50] and tribological advantages of MPC polymers, CLPE-*g*-MPC is believed to be promising for use in the next-generation artificial hip joint systems.

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Erratum

Enhanced Wear Resistance of Orthopaedic Bearing Due to the Cross-Linking of Poly(MPC) Graft Chains Induced by Gamma-Ray Irradiation

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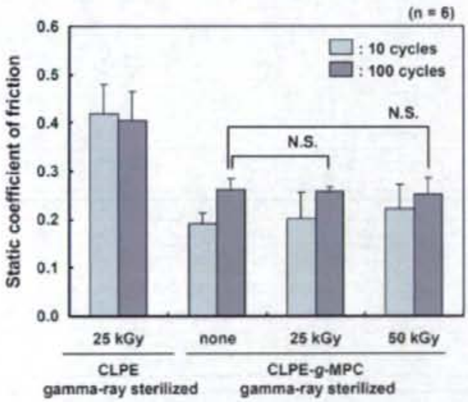

Figure 3. Static coefficients of friction of the gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar, Standard deviations.

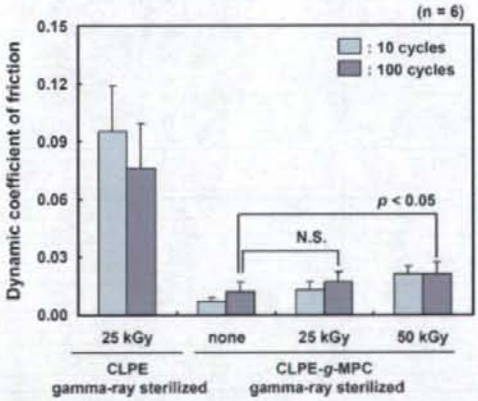

Figure 4. Dynamic coefficients of friction of gamma-ray sterilized CLPE surfaces and nonsterilized and gamma-ray sterilized CLPE-*g*-MPC surfaces. Bar, Standard deviations.

Effect of 2-methacryloyloxyethyl phosphorylcholine concentration on photo-induced graft polymerization of polyethylene in reducing the wear of orthopaedic bearing surface

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Abstract: Photo-induced graft polymerization of 2-methacryloyloxyethyl phosphorylcholine (MPC) on cross-linked polyethylene (CLPE) has been developed as a novel technology for reducing wear of orthopaedic bearings. In this study, the effect of MPC concentration on graft polymerization and the resultant properties of the grafted poly (MPC) layer have been investigated. The grafted poly (MPC) layer thickness increased with the MPC concentration in feed. The hip simulator wear test confirmed that CLPE-*g*-MPC cups exhibited minimal wear compared with untreated CLPE cups. Since MPC is a highly hydrophilic methacrylate, the water-wettability of CLPE-*g*-MPC was greater than that of untreated CLPE due to the formation of a poly(MPC) nanometer-scale layer. The CLPE-*g*-MPC orthopaedic bearing surface exhibited high lubricity, because of the present of the poly(MPC) layer even at a thickness of 10 nm. This layer is considered responsible for the improved wear resistance. Nanometer-scale modification of CLPE with poly(MPC) is expected to significantly increase the durability of the orthopaedic bearings. Poly (MPC) layer thickness can be controlled by changing the MPC concentration in feed. In order to achieve nanometer-scale modification of poly(MPC) in this manner, it is necessary to use a long photo-irradiation time for the MPC graft polymerization system, which contains a high-concentration monomer without its gelation. © 2007 Wiley Periodicals, Inc. J Biomed Mater Res 86A: 439–447, 2008

Key words: joint replacement; polyethylene; phosphorylcholine; graft polymerization; wear mechanism

INTRODUCTION

Polymeric biomaterials are widely used in the biomedical field for manufacturing artificial organs, medical devices, and disposable clinical apparatus.[1,2] The number of artificial hip and knee joints used for primary and revised hip and knee replacement are substantially increasing in the worldwide every year.[3] This indicates that the quality of medical devices such as artificial joints has become increasingly important. The most popular artificial joint system used as a medical device is a bearing couple composed of ultra-high molecular weight polyethylene (UHMWPE) and cobalt–chromium–molybdenum (Co-Cr-Mo) alloy. However, osteolysis caused by the wear particles of UHMWPE in the artificial joint system has emerged as a serious issue.[4,5] Different combinations of bearing surfaces and improvements in bearing materials have been studied with the aim of reducing the number of UHMWPE wear particles inducing osteolysis.[6–9]

Surface modification is important for the improvement of bearing materials. Recently, we developed an artificial hip joint based on a new concept by using 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer grafted onto the surface of cross-linked polyethylene (CLPE; CLPE-*g*-MPC); this device was designed to reduce wear and suppress bone resorp-

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tion.[10–13] MPC, a methacrylate monomer with a phospholipid polar group in the side chain, is a novel biomaterial designed and developed by Ishihara et al., and it mimics the neutral phospholipids of cell membranes.[14] MPC polymers are one of the most common biocompatible and hydrophilic polymers studied thus far, which have potential application in a variety of fields such as biology, biomedical science, and surface chemistry because they possess the unique properties of good biocompatibility, high lubricity and low friction, anti-protein adsorption, and cell membrane-like surface.[15–22]

In general, there are two methods for modifying the polymer surface. The first method involves surface absorption or reaction with small molecules[23–25] and the second, grafting polymeric molecules onto the substrate through covalent bonding.[26] Most frequently, grafting polymerization is performed using either of the following methods: (1) surface-initiated graft polymerization termed as the "grafting from" method in which the monomers are polymerized from initiators or comonomers; and (2) adsorption of the polymer to the substrate termed as the "grafting to" methods (i.e., dipping, cross-linking, and ready-made polymers with reactive end groups reacting with the functional groups of the substrate).[27,28] The "grafting from" method has an advantage over the "grafting to" method in that it synthesizes a high-density polymer brush. The novel artificial joint developed in this study is low-wear bearing with nanometer-scale poly(MPC) surface modification. This surface modification was accomplished by using a photo-induced radical polymerization technique that was similar to that used in the "grafting from" method. However, in this technique, controlling the length and density of the grafted poly(MPC) was difficult.[15] Our previous study confirmed that the density of the grafted poly(MPC) affects wear resistance and that it was controlled by the photo-irradiation time.[12]

In an attempt to resolve another issue in this study, we investigated the effect of MPC concentration variability on photo-induced graft polymerization. The results revealed that it was possible to control the grafted poly(MPC) chains with nanometer scale modification in order to reduce wear of the CLPE-*g*-MPC orthopaedic bearing surface.

MATERIALS AND METHODS

Chemicals

Benzophenone and acetone were purchased from Wako Pure Chemical Industries, (Osaka, Japan). MPC was industrially synthesized using the method reported by Ishihara et al.[14] and supplied by Ai Bio-Chips, (Tokyo, Japan).

MPC graft polymerization

A compression-molded UHMWPE (GUR1020 resin; Poly Hi Solidur, IN, USA) bar stock was irradiated with gamma-ray of 50 kGy in N_2 gas and annealed at 120°C for 7.5 h in N_2 gas in order to attain cross-linking. The CLPE specimens were machined from this bar stock after cooling. The specimens were immersed in an acetone solution containing 10 mg/mL benzophenone for 30 s and then dried in the dark at room temperature to remove acetone. Using ultraviolet spectroscopy, the amount of benzophenone adsorbed on the surface was reported to be 3.5×10^{-11} mol/cm^2 in previous studies.[15,16] The MPC was dissolved in degassed pure water to attain concentrations ranging from 0.06 to 1.00 mol/L. Subsequently, the CLPE specimens coated with benzophenone were immersed in the aqueous MPC solutions. Photo-induced graft polymerization on the CLPE surface was performed using ultraviolet irradiation (UVL-400HA ultra-high pressure mercury lamp; Riko-Kagaku Sangyo, Funabashi, Japan) with an intensity of 5 mW/cm^2 at 60°C for 12–90 min; a filter (Model D-35; Toshiba, Tokyo, Japan) was used restrict the passage of ultraviolet light to wavelengths of 350 ± 50 nm. After polymerization, the CLPE-*g*-MPC specimens were removed, washed with pure water and ethanol, and dried at room temperature. These specimens were then sterilized by 25 kGy gamma-ray under N_2 gas.

Surface analysis by X-ray photoelectron spectroscopy, water-contact angle measurement, and Fourier-transform infrared spectroscopy

The surface elemental contents of CLPE-*g*-MPC obtained with various photo-irradiation times or MPC concentrations were analyzed using X-ray photoelectron spectroscopy (XPS). The XPS spectra were obtained using an XPS spectrophotometer (AXIS Hsi 165; Kratos Analytical, UK) equipped with an Mg-Kα radiation source by applying a voltage of 15 kV at the anode. The take-off angle of the photoelectrons was maintained at 90°. Each measurement was scanned five times, and five replicate measurements were performed on each sample, and the average values were considered for the surface elemental contents.

The static water-contact angles of CLPE-*g*-MPC obtained at various MPC concentrations were measured with an optical bench-type contact angle goniometer (Model DM300; Kyowa Interface Science, Saitama, Japan) using a sessile drop method. Drops of purified water (1 μL) were deposited on the CLPE-*g*-MPC surfaces, and the contact angles were directly measured after 60 s by using a microscope according to the ISO standard 15989.[29] Subsequently, 15 replicate measurements were performed on each sample, and the average values were taken as the contact angles.

The functional group vibrations of the CLPE-*g*-MPC surface that was polymerized with various MPC concentrations were examined using attenuated total reflection (ATR) by Fourier-transform infrared (FTIR) spectroscopy. FTIR/ATR spectra were obtained in 32 scans over a range of 800–2000 cm^{-1} by using an FTIR analyzer (FT/IR615; Jasco International, Tokyo, Japan) at a resolution of 4.0 cm^{-1}.

Cross-sectional observation of CLPE-g-MPC by transmission electron microscopy

A cross-section of the poly(MPC) layer on the CLPE-g-MPC surface produced at various MPC concentrations was observed using a transmission electron microscope (TEM). The specimens were first embedded in epoxy resin, stained with ruthenium oxide vapor at room temperature, and then sliced into ultra-thin films (approximately 100-nm thick) by using a Leica Ultra Cut UC microtome (Leica Microsystems, Wetzlar, Germany). A JEM-1010 electron microscope (JEOL, Tokyo, Japan) was used for the TEM observation at an acceleration voltage of 100 kV.

Surface coated-area observation by Fluorescence Microscopy (FM)

We used rhodamine 6G (Wako Pure Chemical Industries) because it can be easily and rapidly applied to a polymer coating and imaged using fluorescence microscopy (FM) (Axioskop 2 Plus; Carl Zeiss AG, Oberkochen, Germany). Wang et al. observed that rhodamine 6G effectively stains the MPC polymer, which shares very high structural similarity to lipids.[30]

An aqueous solution of 200 mass ppm rhodamine 6G was used for all the staining experiments. All the samples were stained using a two-step procedure. (1) The samples were immersed in the rhodamine 6G solution for 30 s and then removed. (2) Subsequently, they were washed twice consecutively in distilled water for 30 s and dried.

All the samples were examined and imaged using FM. Pseudo-color images were obtained using a charge-coupled-device (CCD) camera (VB-7010; Keyence, Osaka, Japan) and imaging software (VH analyzer 2.51; Keyence). Lenses with a 10× magnification and an appropriate exposure time (approximately 1/10 s) were employed to obtain clear images of the samples.

Friction test

The friction test was performed using a ball-on-plate machine (Tribostation 32; Shinto Scientific, Tokyo, Japan). Each of the CLPE-g-MPC surfaces with various MPC concentrations were used to prepare six sample pieces. A Co-Cr-Mo alloy ball with 9 mm in diameter was prepared. The surface roughness of the ball was Ra = 0.01, which was comparable with that of femoral ball products. The friction tests were performed at room temperature with a load of 0.98 N, sliding distance of 25 mm, and frequency of 1 Hz for a maximum of 100 cycles.[31] Pure water was used as a lubricant. The mean static (μ_s) and dynamic (μ_d) coefficients of friction were determined by averaging five data points from the 100 (96–100) cycle measurements.

Hip simulator wear test

A 12-station hip joint simulator (MTS Systems, MN, USA) with CLPE and CLPE-g-MPC cups both having an inner and outer diameter of 26 and 52 mm, respectively, was used for the hip simulator wear test. For each MPC concentration [0 (untreated), 0.25, and 0.50 mol/L], two sample pieces were prepared. A Co-Cr-Mo alloy femoral ball component with a size of 26 mm (Japan Medical Materials, Osaka, Japan) was used as the femoral component. A mixture of 25 vol % bovine serum, 20 m*M*/L of ethylene diamine tetraacetic acid (EDTA), and 0.1mass % sodium azide was used as a lubricant, according to the ISO standard 14242-1.[32] The lubricant was replaced every 0.5×10^6 cycles. Walks, which simulated a physiologic loading curve (Paul-type) with double peaks at 1793 and 2744 N loads, with a multidirectional (biaxial and orbital) motion of 1 Hz frequency were applied. Wear was determined by weighing the cups at intervals of 0.5×10^6 cycles. Load-soak controls ($n = 2$) were used to compensate the fluid absorption by the specimens.[33] The testing was continued until a total of 5.0×10^6 cycles were completed.

RESULTS

Figure 1 shows the phosphorous (P) concentration of the CLPE-g-MPC surface as a function of the photo-irradiation time during polymerization. The P concentration increased proportionally with the photo-irradiation time. When the photo-irradiation time was greater than 45 min, the P concentration of the CLPE-g-MPC surface with 0.17, 0.25, and 0.50 mol/L MPC concentration became almost constant at high values of 2.9, 3.8, and 4.6 atom %, respectively.

Figure 2 shows the nitrogen (N) and P content in the CLPE-g-MPC surface polymerized with various MPC concentrations and a 90-min photo-irradiation time. Both the N and P content in the CLPE-g-MPC surface increased to 5.2 up to an MPC concentration of 0.50 mol/L; it then gradually decreased with an

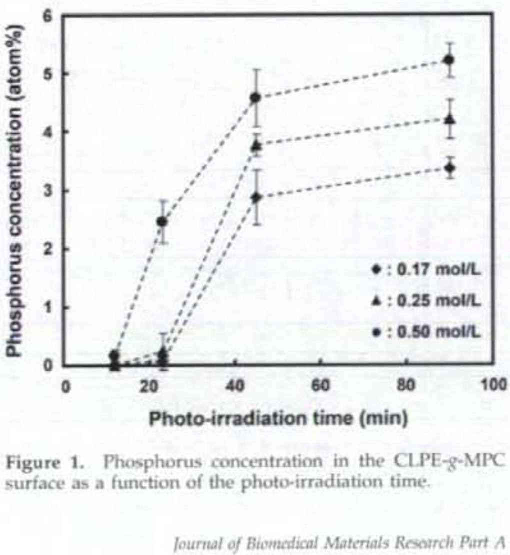

Figure 1. Phosphorus concentration in the CLPE-g-MPC surface as a function of the photo-irradiation time.